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L3: Entry 1 of 4

File: USPT

Aug 7, 2001

US-PAT-NO: 6270765

DOCUMENT-IDENTIFIER: US 6270765 B1

TITLE: Therapeutic compounds comprised of anti-Fc receptor antibodies

DATE-ISSUED: August 7, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Deo; Yashwant M.	Audubon	PA	N/A	N/A
Goldstein; Joel	Edison	NJ	N/A	N/A
Graziano; Robert	Frenchtown	NJ	N/A	N/A
Somasundaram; Chezian	Allentown	PA	N/A	N/A

US-CL-CURRENT: 424/136.1; 424/134.1, 424/135.1, 424/178.1, 424/192.1,
424/193.1, 424/277.1, 435/69.1, 514/12, 530/387.3

Full	Title	Citation	Front	Review	Classification	Date	Reference	Claims	KWIC	Draw Desc	Image
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☐ 2. Document ID: US 6018031 A

L3: Entry 2 of 4

File: USPT

Jan 25, 2000

US-PAT-NO: 6018031

DOCUMENT-IDENTIFIER: US 6018031 A

TITLE: Binding agents specific for IgA receptor

DATE-ISSUED: January 25, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Shen; Lilian	Thetford Center	VT	N/A	N/A
Fanger; Michael W.	Lebanon	NH	N/A	N/A

US-CL-CURRENT: 530/387.3; 530/387.7, 530/388.2, 530/388.22

Full	Title	Citation	Front	Review	Classification	Date	Reference	Claims	KWIC	Draw Desc	Image
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☐ 3. Document ID: US 5849708 A

L3: Entry 3 of 4

File: USPT

Dec 15, 1998

US-PAT-NO: 5849708

DOCUMENT-IDENTIFIER: US 5849708 A

TITLE: Promotion of eating behavior

DATE-ISSUED: December 15, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Maratos-Flier; Eleftheria	Newton	MA	N/A	N/A

US-CL-CURRENT: 514/13; 530/300, 530/317

Full	Title	Citation	Front	Review	Classification	Date	Reference	Claims	KMC	Draw Desc	Image
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☐ 4. Document ID: US 5837243 A

L3: Entry 4 of 4

File: USPT

Nov 17, 1998

US-PAT-NO: 5837243

DOCUMENT-IDENTIFIER: US 5837243 A

TITLE: Therapeutic compounds comprised of anti-Fc receptor antibodies

DATE-ISSUED: November 17, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Deo; Yashwant M.	Audubon	PA	N/A	N/A
Goldstein; Joel	Edison	NJ	N/A	N/A
Graziano; Robert	Frenchtown	NJ	N/A	N/A
Somasundaram; Chezian	Allentown	PA	N/A	N/A

US-CL-CURRENT: 424/136.1; 424/134.1, 424/135.1, 424/184.1, 424/192.1,
424/277.1, 512/12, 530/387.3

Full	Title	Citation	Front	Review	Classification	Date	Reference	KMC	Draw Desc	Image
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Terms	Documents
(altered adj peptide\$3) with administ\$6	4

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Search Results - Record(s) 1 through 4 of 4 returned.☐ 1. Document ID: US 6270765 B1

L3: Entry 1 of 4

File: USPT

Aug 7, 2001

DOCUMENT-IDENTIFIER: US 6270765 B1

TITLE: Therapeutic compounds comprised of anti-Fc receptor antibodies

DEPR:

In another embodiment of the invention, a multispecific molecule comprises an antigen that has been modified, such that its effect on T cell activation is modified upon presentation of the modified antigen to the T cell by an antigen presenting cell. Allan et al. have in fact shown that substitution of one or more amino acids of a peptide that stimulates T cells, e.g., stimulates T cell proliferation, can result in an antigen which fails to stimulate the T cell or which induces anergy in the T cell. Such modified peptides are termed Altered Peptide Ligands (APL). Accordingly, such APLs can be linked to bispecific or multispecific molecules having at least one binding specificity for the Fc.gamma.RI. Upon phagocytosis of these molecules by antigen presenting cells and presentation to T cells, the proliferation of the T cells may be inhibited or anergized. Accordingly, administration to a subject of a multispecific molecule comprising (a) at least one altered peptide of an antigen which normally stimulates T cells, but which upon modification induces anergy of the T cells, and (b) at least one anti-Fc.gamma.RI antibody will result in induction of tolerance of the subject to the antigen. Thus, such multi- or bispecific molecules can be used to tolerize a subject to a variety of antigens, e.g., auto-antigens. Thus, depending on the antigen used, the methods of the invention provide methods for increasing an immune response, i.e., by using an antigen which stimulates T cells, and the invention also provides methods for reducing an immune response, either by inhibiting T cell stimulation or by inducing anergy of the T cells.

Full	Title	Citation	Front	Review	Classification	Date	Reference
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KWIC	Draw Desc	Image
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☐ 2. Document ID: US 6018031 A

L3: Entry 2 of 4

File: USPT

Jan 25, 2000

DOCUMENT-IDENTIFIER: US 6018031 A
TITLE: Binding agents specific for IgA receptor

BSPR:

In another embodiment of the invention, a binding agent is linked to an antigen that has been modified, such that its effect on T cell activation is modified upon presentation of the modified antigen to the T cell by an antigen presenting cell. Allan et al. have in fact shown that substitution of one or more amino acids of a peptide that stimulates T cells, e.g., stimulates T cell proliferation, can result in an antigen which fails to stimulate the T cell or which induces anergy in the T cell. Such modified peptides are termed Altered Peptide Ligands (APL). Accordingly, such APLs can be linked to binding agents of the invention, e.g., bispecific or multispecific molecules having at least one binding specificity for the Fc.gamma. RI. Upon phagocytosis of these molecules by antigen presenting cells and presentation to T cells, the proliferation of the T cells may be inhibited or anergized. Accordingly, administration to a subject of a binding agent comprising (a) at least one altered peptide of an antigen which normally stimulates T cells, but which upon modification induces anergy of the T cells, and (b) at least one antigen binding region specific for an Fc.alpha.R can result in induction of tolerance of the subject to the antigen. Thus, such binding agents of the invention can be used to tolerize a subject to a variety of antigens, e.g., auto-antigens. Thus, depending on the antigen used, the methods of the invention provide methods for increasing an immune response, i.e., by using an antigen which stimulates T cells, and the invention also provides methods for reducing an immune response, either by inhibiting T cell stimulation or by inducing anergy of the T cells.

Full	Title	Citation	Front	Review	Classification	Date	Reference
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KWIC	Draw Desc	Image
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☐ 3. Document ID: US 5849708 A

L3: Entry 3 of 4

File: USPT

Dec 15, 1998

DOCUMENT-IDENTIFIER: US 5849708 A
TITLE: Promotion of eating behavior

BSPR:

In another aspect, the invention features a method of making an MCH polypeptide, e.g., a MCH polypeptide having a non-wild type activity, e.g., an antagonist, agonist or super agonist of a naturally occurring MCH. The method includes: altering the sequence or ring structure of an MCH peptide, preferably a mammalian, e.g., a human or rat peptide, or a peptide other than a fish, amphibian or reptilian peptide, and testing the altered peptide for the desired activity, e.g., by administering it to an animal and determining its effect on MCH RNA or protein levels, eating behavior or weight.

Full	Title	Citation	Front	Review	Classification	Date	Reference
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KWIC	Draw Desc	Image
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☐ 4. Document ID: US 5837243 A

L3: Entry 4 of 4

File: USPT

Nov 17, 1998

DOCUMENT-IDENTIFIER: US 5837243 A

TITLE: Therapeutic compounds comprised of anti-Fc receptor antibodies

DEPR:

In another embodiment of the invention, a multispecific molecule comprises an antigen that has been modified, such that its effect on T cell activation is modified upon presentation of the modified antigen to the T cell by an antigen presenting cell. Allan et al. have in fact shown that substitution of one or more amino acids of a peptide that stimulates T cells, e.g., stimulates T cell proliferation, can result in an antigen which fails to stimulate the T cell or which induces anergy in the T cell. Such modified peptides are termed Altered Peptide Ligands (APL). Accordingly, such APLs can be linked to bispecific or multispecific molecules having at least one binding specificity for the Fc.gamma.RI. Upon phagocytosis of these molecules by antigen presenting cells and presentation to T cells, the proliferation of the T cells may be inhibited or anergized. Accordingly, administration to a subject of a multispecific molecule comprising (a) at least one altered peptide of an antigen which normally stimulates T cells, but which upon modification induces anergy of the T cells, and (b) at least one anti-Fc.gamma.RI antibody will result in induction of tolerance of the subject to the antigen. Thus, such multi- or bispecific molecules can be used to tolerize a subject to a variety of antigens, e.g., auto-antigens. Thus, depending on the antigen used, the methods of the invention provide methods for increasing an immune response, i.e., by using an antigen which stimulates T cells, and the invention also provides methods for reducing an immune response, either by inhibiting T cell stimulation or by inducing anergy of the T cells.

Full	Title	Citation	Front	Review	Classification	Date	Reference
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KWIC	Draw Desc	Image
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Terms	Documents
(altered adj peptide\$3) with administ\$6	4

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USPT,PGPB,JPAB,EPAB,DWPI	(Landry Samuel J)[IN] AND MHC and peptide	644	<u>L13</u>
USPT,PGPB,JPAB,EPAB,DWPI	(Landry Sam\$)[IN] AND MHC and peptide	2	<u>L12</u>
USPT,PGPB,JPAB,EPAB,DWPI	(Landry Sam\$)[IN] AND MHC and peptide and immun\$6 and alter\$8	2	<u>L11</u>
USPT,PGPB,JPAB,EPAB,DWPI	(Landry S\$)[IN] AND MHC and peptide and immun\$6 and alter\$8	165	<u>L10</u>
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USPT,PGPB,JPAB,EPAB,DWPI	(Landry S\$)[IN] AND MHC and peptide and immun\$^	0	<u>L8</u>
USPT,PGPB,JPAB,EPAB,DWPI	(Landry S\$)[IN] AND MHC and peptide	286	<u>L7</u>
USPT,PGPB,JPAB,EPAB,DWPI	(Landry S\$)[IN] AND MHC and peptid	2	<u>L6</u>
USPT,PGPB,JPAB,EPAB,DWPI	(Landry S\$)[IN] AND MHC	439	<u>L5</u>
USPT,PGPB,JPAB,EPAB,DWPI	(Landry S\$)[IN] AND (peptide\$3)	9501	<u>L4</u>
USPT,PGPB,JPAB,EPAB,DWPI	(altered adj peptide\$3) with administ\$6	4	<u>L3</u>
USPT,PGPB,JPAB,EPAB,DWPI	(altered adj peptide\$3) withadminist\$6	87	<u>L2</u>
USPT,PGPB,JPAB,EPAB,DWPI	(altered adj peptide\$3) near administ\$6	0	<u>L1</u>

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2 FILES SEARCHED...
3 FILES SEARCHED...
L2 416 L1 AND PD<19980728

=> s l2 (10N) administ?
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L6 (10A) ADMINIST?'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L7 (10A) ADMINIST?'
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FIELD CODE - 'AND' OPERATOR ASSUMED 'L8 (10A) ADMINIST?'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L9 (10A) ADMINIST?'
L3 21 L2 (10N) ADMINIST?

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PROCESSING COMPLETED FOR L3
L4 11 DUP REM L3 (10 DUPLICATES REMOVED)

=> dis l4 1-11 ibib abs kwic

L4 ANSWER 1 OF 11 CAPLUS COPYRIGHT 2001 ACS DUPLICATE 1
ACCESSION NUMBER: 1998:441443 CAPLUS
DOCUMENT NUMBER: 129:174345
TITLE: Antigen-based T-cell-targeted immunotherapy: recent
developments in autoimmunity and allergy
AUTHOR(S): Stemmer, Christine; Guichard, Gilles
CORPORATE SOURCE: UPR 9021 CNRS, Immunochimie des peptides et des virus,
Institut de Biologie Moleculaire et Cellulaire,
Strasbourg, 67000, Fr.
SOURCE: Expert Opin. Ther. Pat. (1998), 8(7),
819-830
CODEN: EOTPEG; ISSN: 1354-3776
PUBLISHER: Ashley Publications
DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review with 125 refs. In the past few years, there has been intense effort in the design of antigen-based strategies for T-cell-targeted immunotherapy in autoimmunity and allergy. The administration of peptide or protein antigens to induce specific T-cell tolerance has been evaluated critically in a no. of animal models and clin. trials. Also promising is the use of altered peptide ligands (APL) to promote immune deviations. Recent advances in the field of hapten recognition by T-cells suggest the use of MHC binding peptide:hapten conjugates to treat hapten-mediated hypersensitivities. Alternatively, induction of tolerance can be achieved via the administration of sol. MHC mol./peptide complexes. Finally, the design of inhibitors that block peptide binding to MHC mols. has experienced a renewal of interest, in particular with the patented discovery of new high affinity low mol. wt. MHC class II restricted ligands. This review covers patent activity over the past 19 mo in these fields in the light of recent literature.

SO Expert Opin. Ther. Pat. (1998), 8(7), 819-830

CODEN: EOTPEG; ISSN: 1354-3776

AB A review with 125 refs. In the past few years, there has been intense effort in the design of antigen-based strategies for T-cell-targeted immunotherapy in autoimmunity and allergy. The administration of peptide or protein antigens to induce specific T-cell tolerance has been evaluated critically in a no. of animal models and clin. trials. Also promising is the use of altered peptide ligands (APL) to promote immune deviations. Recent advances in the field of hapten recognition by T-cells suggest the use of MHC binding peptide:hapten conjugates to treat hapten-mediated hypersensitivities. Alternatively, induction of tolerance can be achieved via the administration of sol. MHC mol./peptide complexes. Finally, the design of inhibitors that block peptide binding to MHC mols. has experienced a renewal of interest, in particular with the patented discovery of new high affinity low mol. wt. MHC class II restricted ligands. This review covers patent activity over the past 19 mo in these fields in the light of recent literature.

L4 ANSWER 2 OF 11 CAPLUS COPYRIGHT 2001 ACS DUPLICATE 2

ACCESSION NUMBER: 1998:681381 CAPLUS

DOCUMENT NUMBER: 130:80237

TITLE: Heat-shock protein T-cell epitopes trigger a spreading regulatory control in a diversified arthritogenic T-cell response

AUTHOR(S): Van Eden, Willem; Van Der Zee, Ruurd; Taams, Leonie S.; Prakken, A. Berent J.; Van Roon, Joel; Wauben, Marca H. M.

CORPORATE SOURCE: Institute of Infectious Diseases and Immunology, Veterinary Faculty, University of Utrecht, Utrecht, 3584 CL, Neth.

SOURCE: Immunol. Rev. (1998), 164, 169-174

CODEN: IMRED2; ISSN: 0105-2896

PUBLISHER: Munksgaard International Publishers Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Adjuvant arthritis (AA) in Lewis rats is T-cell mediated and seems to depend on T cells recognizing the 180-188 epitope of mycobacterial heat-shock protein (hsp) 60. Anal. of arthritogenic T-cell clone A2b has revealed a mimicry of this particular epitope with an articular cartilage-assocd. target T-cell epitope. Nasal administration of synthetic peptides covering this 180-188 sequence led to epitope-specific tolerance and resistance to AA. Since this tolerization protocol also inhibited avridine arthritis, one may conclude that this form of epitope-specific tolerance had effectuated a spreading tolerization at the level of target antigens that included a diverse set of possible arthritis-assocd. antigens. In vitro anergized T cells exhibited suppressive activity in a co-culture system. As in this case, depending on the presence of the antigen of the anergic T cell, such T cells suppressed responder T cells of a different antigenic specificity, the authors postulated that anergic T cells may be responsible for a spreading of tolerance. It seemed that such spreading of tolerance was channeled through the antigen-presenting cells (APC) and was dependent on direct cell-cell contact. This and addnl. forms of spreading of tolerance could be responsible for specific nasal tolerance, causing inhibition of the development of an arthritogenic inflammatory response. This can be similarly the case for the arthritis protection that resulted from immunization with hsp. Anal. of T-cell responses following hsp immunizations revealed that the arthritis inhibitory activity resided in T cells with specificity for a conserved part of microbial hsp60. The same T cells cross-responded to rat self-hsp60. Low level expression of the latter mol. on non-professional APC could possibly have induced a suppressive anergic state in these autoreactive cells. Thus, immunization with microbial hsp would have led to an expansion of such T cells, leading to raised disease-suppressive potential when selectively trapped and activated in the inflamed self-hsp-overexpressing joint. Alternatively, the cross-recognized self-hsp epitope could have the regulatory qualities of an altered peptide ligand or a partial agonist for T cells that see the microbial homolog as the full agonist.

REFERENCE COUNT: 23

REFERENCE(S): (1) Alam, A; J Immunol 1996, V156, P3480 CAPLUS
(2) Anderton, S; J Exp Med 1995, V181, P943 CAPLUS
(3) Birk, O; Proc Natl Acad Sci USA 1996, V93, P1032 CAPLUS
(4) Boog, C; J Exp Med 1992, V175, P1805 CAPLUS
(5) Broeren, C; Immunology 1995, V84, P193 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

SO Immunol. Rev. (1998), 164, 169-174

CODEN: IMRED2; ISSN: 0105-2896

AB Adjuvant arthritis (AA) in Lewis rats is T-cell mediated and seems to depend on T cells recognizing the 180-188 epitope of mycobacterial heat-shock protein (hsp) 60. Anal. of arthritogenic T-cell clone A2b has revealed a mimicry of this particular epitope with an articular cartilage-assocd. target T-cell epitope. Nasal administration of synthetic peptides covering this 180-188 sequence led to epitope-specific tolerance and resistance to AA. Since this tolerization protocol also inhibited avridine arthritis, one may conclude that this form of epitope-specific tolerance had effectuated a spreading tolerization at the level of target antigens that included a diverse set of possible arthritis-assocd. antigens. In vitro anergized T cells exhibited suppressive activity in a co-culture system. As in this case, depending on the presence of the antigen of the anergic T cell, such T cells suppressed responder T cells of a different antigenic specificity, the authors postulated that anergic T cells may be responsible for a spreading of tolerance. It seemed that such spreading of tolerance was channeled through the antigen-presenting cells (APC) and was dependent on

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L4 ANSWER 3 OF 11 BIOSIS COPYRIGHT 2001 BIOSIS

ACCESSION NUMBER: 1998:434206 BIOSIS

DOCUMENT NUMBER: PREV199800434206

TITLE: A gene therapy approach to treatment of autoimmune disease.

AUTHOR(S): Seroogy, Christine M. (1); Fathman, C. Garrison

CORPORATE SOURCE: (1) Dep. Med., Div. Rheumatol. Immunol., Stanford Univ.,

300 Pasteur Dr., Rm S021, Stanford, CA 94305-5111 USA

SOURCE: Immunologic Research, (Aug., 1998) Vol. 18, No.

1, pp. 15-26.

ISSN: 0257-277X.

DOCUMENT TYPE: General Review

LANGUAGE: English

AB New insights into the underlying mechanisms for the development of autoimmune diseases in humans and various animal models continue to increase with our understanding of factors that drive polarization of T helper (Th) responses and tolerance. This information has led to the development of new treatment strategies, including oral tolerance clinical trials and the use of altered peptide ligands in animal models. These approaches have shown some promise and provided additional insight into the disease processes. The use of gene therapy in many disease states continues to increase. We are starting to see the application of gene therapy in chronic diseases in humans. Gene therapy has been used in several animal models of autoimmune disease with promising preliminary results. In this article, an overview will be provided for the use of gene therapy in autoimmune disease.

SO Immunologic Research, (Aug., 1998) Vol. 18, No. 1, pp. 15-26.

ISSN: 0257-277X.

AB. . . This information has led to the development of new treatment strategies, including oral tolerance clinical trials and the use of altered peptide ligands in animal models. These approaches have shown some promise and provided additional insight into the disease processes. The use. . .

IT Methods & Equipment

gene therapy: therapeutic method; oral antigen administration

: therapeutic method; systemic antigen administration:

therapeutic method

IT Miscellaneous Descriptors

immune tolerance; T helper response

L4 ANSWER 4 OF 11 CAPLUS COPYRIGHT 2001 ACS

DUPLICATE 3

ACCESSION NUMBER: 1997:752175 CAPLUS

DOCUMENT NUMBER: 128:83926

TITLE: Antigen-specific therapies for the treatment of

multiple sclerosis: a clinical trial update

AUTHOR(S): Spack, Edward G.

CORPORATE SOURCE: Department of Immunology, Anergen, Inc., Redwood City,

CA, 94063, USA

SOURCE: Expert Opin. Invest. Drugs (1997), 6(11),

1715-1727

CODEN: EOIDER; ISSN: 0967-8298

PUBLISHER: Ashley Publications

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review with 75 refs. Within the past year a host of antigen-specific therapies for multiple sclerosis (MS) progressed along the path from IND submission to FDA approval. The Immune Response Corp. vaccinated patients with a V.beta.6 peptide, demonstrating that the vaccine was immunogenic, well-tolerated, and reduced the no. of V.beta.6+ T-cells in the cerebrospinal fluid (CSF). Connetics conducted a Phase I/II trial on chronic progressive MS patients vaccinated with CDR2 peptides from TCR V.beta.55.2 and found that patients with a measurable response to the vaccine remained clin. stable for a year. A study at the University of Alberta MS Patient Care and Research Clinic demonstrated that it. Injection of a B-cell/T-cell epitope of myelin basic protein (MBP) decreased the level of anti-MBP antibody, but i.v. administration did not decrease the relapse rate. AutoImmune completed a Phase III trial of oral myelin in the spring of 1997 which failed to show a statistical difference between those patients fed placebo and those fed daily capsules of myelin protein (Myoral). Three Phase I trials of i.v. myelin antigen(s) were initiated: MP4 (Alexion Pharmaceuticals), a recombinant fusion of myelin basic protein and proteolipid protein; AG284 (Anergen), a solubilized HLA-DR2:MBP peptide complex; and NBI-5788 (Neurocrine Biosciences), an altered peptide ligand of an immunodominant MBP T-cell epitope. Following the conclusion of a successful Phase III clin. trial, TEVA Pharmaceutical Industries received FDA approval to market Copaxone (glatiramer acetate) for the treatment of relapsing-remitting MS in Dec. of 1996 and launched the product in 1997. The recent preclin. research and clin. trial status of these antigen-specific MS therapeutics are summarized in this review.

SO Expert Opin. Invest. Drugs (1997), 6(11), 1715-1727

CODEN: EOIDER; ISSN: 0967-8298

AB A review with 75 refs. Within the past year a host of antigen-specific therapies for multiple sclerosis (MS) progressed along the path from IND submission to FDA approval. The Immune Response Corp. vaccinated patients with a V.beta.6 peptide, demonstrating that the vaccine was immunogenic, well-tolerated, and reduced the no. of V.beta.6+ T-cells in the cerebrospinal fluid (CSF). Connetics conducted a Phase I/II trial on chronic progressive MS patients vaccinated with CDR2 peptides from TCR V.beta.55.2 and found that patients with a measurable response to the vaccine remained clin. stable for a year. A study at the University of Alberta MS Patient Care and Research Clinic demonstrated that it. Injection of a B-cell/T-cell epitope of myelin basic protein (MBP) decreased the level of anti-MBP antibody, but i.v. administration did not decrease the relapse rate. AutoImmune completed a Phase III trial of oral myelin in the spring of 1997 which failed to show a statistical difference between those patients fed placebo and those fed daily capsules

of myelin protein (Myoral). Three Phase I studies of i.v. myelin antigen(s) were initiated: MP4 (Alexion Pharmaceuticals), a recombinant fusion of myelin basic protein and proteolipid protein; AG284 (Anergen), a solubilized HLA-DR2:MBP peptide complex; and NBI-5788 (Neurocrine Biosciences), an altered peptide ligand of an immunodominant MBP T-cell epitope. Following the conclusion of a successful Phase III clin. trial, TEVA Pharmaceutical Industries received FDA approval to market Copaxone (glatiramer acetate) for the treatment of relapsing-remitting MS in Dec. of 1996 and launched the product in 1997. The recent preclin. research and clin. trial status of these antigen-specific MS therapeutics are summarized in this review.

L4 ANSWER 5 OF 11 CAPLUS COPYRIGHT 2001 ACS DUPLICATE 4
 ACCESSION NUMBER: 1997:177845 CAPLUS
 DOCUMENT NUMBER: 126:250082
 TITLE: Amelioration of relapsing experimental autoimmune encephalomyelitis with altered myelin basic protein peptides involves different cellular mechanisms
 AUTHOR(S): Gaur, Amitabh; Boehme, Stefan A.; Chalmers, Derek; Crowe, Paul D.; Pahuja, Anil; Ling, Nicholas; Brocke, Stefan; Steinman, Lawrence; Conlon, Paul J.
 CORPORATE SOURCE: Neurocrine Biosciences, 3050 Science Park Road, San Diego, CA, 92121, USA
 SOURCE: J. Neuroimmunol. (1997), 74(1,2), 149-158
 CODEN: JNRIDW; ISSN: 0165-5728
 PUBLISHER: Elsevier
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB T-cells specific for a region of human myelin basic protein, amino acids 87-99 (hMBP87-99), have been implicated in the development of multiple sclerosis (MS) a demyelinating disease of the central nervous system. Administration of sol. altered peptide ligand (APL), made by substituting native residues with alanine at either positions 91(91K>A or A91) or 97 (97R>A or A97) in the hMBP87-99 peptide, blocked the development of chronic relapsing exptl. autoimmune encephalomyelitis (R-EAE), in the SJL mouse. The non-encephalitogenic APL A91, appears to induce cytokine shifts from Th1 to Th2 in the target T-cells, whereas the encephalitogenic superagonist APL A97 causes deletion of the MBP87-99 responsive cells. Thus, single amino acid changes at different positions in the same peptide epitope can lead to APL capable of controlling autoimmune disease by different mechanisms.

SO J. Neuroimmunol. (1997), 74(1,2), 149-158
 CODEN: JNRIDW; ISSN: 0165-5728

AB T-cells specific for a region of human myelin basic protein, amino acids 87-99 (hMBP87-99), have been implicated in the development of multiple sclerosis (MS) a demyelinating disease of the central nervous system. Administration of sol. altered peptide ligand (APL), made by substituting native residues with alanine at either positions 91(91K>A or A91) or 97 (97R>A or A97) in the hMBP87-99 peptide, blocked the development of chronic relapsing exptl. autoimmune encephalomyelitis (R-EAE), in the SJL mouse. The non-encephalitogenic APL A91, appears to induce cytokine shifts from Th1 to Th2 in the target T-cells, whereas the encephalitogenic superagonist APL A97 causes deletion of the MBP87-99 responsive cells. Thus, single amino acid changes at different positions in the same peptide epitope can lead to APL capable of controlling autoimmune disease by different mechanisms.

L4 ANSWER 6 OF 11 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.DUPLICATE 5
 ACCESSION NUMBER: 97372086 EMBASE
 DOCUMENT NUMBER: 1997372086
 TITLE: Mucosal tolerance: A two-edged sword to prevent and treat autoimmune diseases.
 AUTHOR: Xiao B.-G.; Link H.
 CORPORATE SOURCE: B.-G. Xiao, Division of Neurology, Karolinska Institute, Huddinge University Hospital, Stockholm, Sweden
 SOURCE: Clinical Immunology and Immunopathology, (1997) 85/2 (119-128).
 Refs: 59
 ISSN: 0090-1229 CODEN: CLIIAT
 COUNTRY: United States
 DOCUMENT TYPE: Journal; General Review
 FILE SEGMENT: 026 Immunology, Serology and Transplantation
 LANGUAGE: English
 SUMMARY LANGUAGE: English

AB Mucosal administration of autoantigens results in the development of a state of peripheral immunological tolerance. Depending upon the dose of antigen administered, anergy/deletion of antigen-specific T cells (higher doses) and/or selective expansion of cells producing immunosuppressive cytokines (TGF- β , IL-4, and IL-10) (lower doses) are two major mechanisms in mucosal tolerance induction. Mucosal tolerance is more effective after nasal compared to oral administration of antigens at the same dose. A large series of studies have demonstrated that mucosal tolerance by oral or nasal antigen administration effectively prevents several experimental disease models (EAE, EAMG, EAN, EAU, IDDM, and CIA). Mucosal antigen administration is superior in prevention to treatment of autoimmune diseases. To broaden the effectiveness of mucosal tolerance, a conjunction of tolerogens with cytokines/CTB might enhance suppression of clinical disease. Based on experimental experience with mucosal tolerance, trials in humans are ongoing in MS, RA, and uveitis. However, mucosal tolerance induction is related to the route of antigen administration (oral, nasal, parenteral), type of antigen (whole protein, peptide, altered peptide), and timing with regard to disease onset and may represent a two-edged sword. In particular, the risks of worsening an ongoing autoimmune disease by mucosal antigen administration have been incompletely addressed. Here we give an overview on some recent developments in this field where, however, much more studies are needed to define an ultimate and safe procedure.

SO Clinical Immunology and Immunopathology, (1997) 85/2 (119-128).
 Refs: 59
 ISSN: 0090-1229 CODEN: CLIIAT

AB Mucosal administration of autoantigens results in the development of a state of peripheral immunological tolerance. Depending upon the dose of antigen administered, anergy/deletion of antigen-specific T cells (higher doses) and/or selective expansion of cells producing immunosuppressive cytokines (TGF- β , IL-4, and IL-10) (lower doses) are two major mechanisms in mucosal tolerance induction. Mucosal tolerance is more effective after nasal compared to oral administration of antigens at the same dose. A large series of studies have demonstrated that mucosal tolerance by oral or nasal antigen administration effectively prevents several experimental disease models (EAE, EAMG, EAN, EAU, IDDM, and CIA). Mucosal antigen

administration is superior in prevention to treatment of autoimmune diseases. To broaden the effectiveness of mucosal tolerance, a conjunction of tolerogens. . . . in humans are ongoing in MS, RA, and uveitis. However, mucosal tolerance induction is related to the route of antigen administration (oral, nasal, parenteral), type of antigen (whole protein, peptide, altered peptide), and timing with regard to disease onset and may represent a two-edged sword. In particular, the risks of worsening an ongoing autoimmune disease by mucosal antigen administration have been incompletely addressed. Here we give an overview on some recent developments in this field where, however, much more. . . .

L4 ANSWER 7 OF 11 CAPLUS COPYRIGHT 2001 ACS DUPLICATE 6
 ACCESSION NUMBER: 1996:180731 CAPLUS
 DOCUMENT NUMBER: 124:229209
 TITLE: A few autoreactive cells in an autoimmune infiltrate control a vast population of nonspecific cells: a tale of smart bombs and the infantry
 AUTHOR(S): Steinman, Lawrence
 CORPORATE SOURCE: Dep. Immunol., Weizmann Inst. Sci., Rehovot, Israel
 SOURCE: Proc. Natl. Acad. Sci. U. S. A. (1996), 93(6), 2253-6
 CODEN: PNASAG; ISSN: 0027-8424
 DOCUMENT TYPE: Journal; General Review
 LANGUAGE: English
 AB A review with 26 refs. Inflammatory infiltrates in tissue-specific autoimmune disease comprise a collection of T cells with specificity for an antigen in the target organ. These specific cells recruit a population of nonspecific T cells and macrophages. The rare tissue-specific T cells in the infiltrate have the capacity to regulate both the influx and the efflux of cells from the tissue. Administration of an altered peptide ligand for the specific T cell which triggers autoimmunity can lead to the regression of the entire inflammatory ensemble in a few hours. Interleukin 4 is a crit. cytokine involved in the regression of the inflammatory infiltrate.
 SO Proc. Natl. Acad. Sci. U. S. A. (1996), 93(6), 2253-6
 CODEN: PNASAG; ISSN: 0027-8424
 AB A review with 26 refs. Inflammatory infiltrates in tissue-specific autoimmune disease comprise a collection of T cells with specificity for an antigen in the target organ. These specific cells recruit a population of nonspecific T cells and macrophages. The rare tissue-specific T cells in the infiltrate have the capacity to regulate both the influx and the efflux of cells from the tissue. Administration of an altered peptide ligand for the specific T cell which triggers autoimmunity can lead to the regression of the entire inflammatory ensemble in a few hours. Interleukin 4 is a crit. cytokine involved in the regression of the inflammatory infiltrate.

L4 ANSWER 8 OF 11 CAPLUS COPYRIGHT 2001 ACS DUPLICATE 7
 ACCESSION NUMBER: 1997:37708 CAPLUS
 DOCUMENT NUMBER: 126:73547
 TITLE: Altered peptide ligands of a myasthenogenic epitope as modulators of specific T-cell responses
 AUTHOR(S): Kirshner, S. L.; Zisman, E.; Fridkin, M.; Sela, M.; Mozes, E.
 CORPORATE SOURCE: Department of Immunology, The Weizmann Institute of Science, Rehovot, Israel
 SOURCE: Scand. J. Immunol. (1996), 44(5), 512-521
 CODEN: SJIMAX; ISSN: 0300-9475
 PUBLISHER: Blackwell
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB Myasthenia gravis (MG) is a T-cell regulated autoimmune disease. A peptide representing a sequence of the human acetylcholine receptor .alpha.-subunit (p195-212) was previously shown to stimulate proliferative responses of peripheral blood lymphocytes from MG patients and to be an immunodominant and myasthenogenic T-cell epitope in SJL mice. The authors generated a panel of analogs of p195-212 that contain single amino acid substitutions. Three of the analogs (203PHE, 204GLY and 207ALA) triggered low to no proliferative responses of a p195-212-specific T-cell line designated TCSJL195-212. Two of these analogs were able to stimulate the line to produce interleukin-2 (IL-2) and IL-4 (203PHE and 204GLY), whereas one analog, 207ALA, did not stimulate the line to produce these cytokines. Binding assays revealed that the binding affinity of an altered peptide for a given major histocompatibility complex (MHC) mol. is not sufficient to det. whether it will be stimulatory or inhibitory to a native peptide-specific T-cell line. Two of the analogs, 204GLY and 207ALA, inhibited proliferative responses of cells of the TCSJL195-212 line when co-cultured with p195-212 and syngeneic antigen presenting cells (APC). The two inhibitory analogs were also able to inhibit proliferative responses of the TCSJL195-212 line when APC were pre-pulsed with p195-212, indicating that MHC blockade is not the only mechanism of action of these peptides. Moreover, both analogs inhibited the ability of p195-212 to prime lymph node cells for proliferative responses even when the analogs were administered in a sol. form. Thus the altered peptide ligands 207ALA and 204GLY can modulate T-cell responses both in vitro and in vivo and may have therapeutic potential for the treatment of MG.
 TI Altered peptide ligands of a myasthenogenic epitope as modulators of specific T-cell responses
 SO Scand. J. Immunol. (1996), 44(5), 512-521
 CODEN: SJIMAX; ISSN: 0300-9475
 AB Myasthenia gravis (MG) is a T-cell regulated autoimmune disease. A peptide representing a sequence of the human acetylcholine receptor .alpha.-subunit (p195-212) was previously shown to stimulate proliferative responses of peripheral blood lymphocytes from MG patients and to be an immunodominant and myasthenogenic T-cell epitope in SJL mice. The authors generated a panel of analogs of p195-212 that contain single amino acid substitutions. Three of the analogs (203PHE, 204GLY and 207ALA) triggered low to no proliferative responses of a p195-212-specific T-cell line designated TCSJL195-212. Two of these analogs were able to stimulate the line to produce interleukin-2 (IL-2) and IL-4 (203PHE and 204GLY), whereas one analog, 207ALA, did not stimulate the line to produce these cytokines. Binding assays revealed that the binding affinity of an altered peptide for a given major histocompatibility complex (MHC) mol. is not sufficient to det. whether it will be stimulatory or inhibitory to a native peptide-specific T-cell line. Two of the analogs, 204GLY and 207ALA, inhibited proliferative responses of cells of the TCSJL195-212 line when co-cultured with p195-212 and syngeneic antigen presenting cells (APC). The two inhibitory analogs were also able to inhibit proliferative responses of the TCSJL195-212 line when APC were pre-pulsed with p195-212, indicating that MHC blockade is not the only mechanism of action of these

peptides. Moreover, both analogs inhibited ability of p195-212 to prime lymph node cells for proliferative responses even when the analogs were administered in a sol. form. Thus the altered peptide ligands 207ALA and 204GLY can modulate T-cell responses both in vitro and in vivo and may have therapeutic potential for the treatment of MG.

L4 ANSWER 9 OF 11 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 91285959 EMBASE
DOCUMENT NUMBER: 1991285959
TITLE: Anti-inflammatory activity of .alpha.-MSH(11-13) analogs: Influences of alteration in stereochemistry.
AUTHOR: Hiltz M.E.; Catania A.; Lipton J.M.
CORPORATE SOURCE: Department of Physiology, University of Texas, Southwestern Med. Ctr Dallas, 5323 Harry Hines Boulevard, Dallas, TX 75235-9040, United States
SOURCE: Peptides, (1991) 12/4 (767-771).
ISSN: 0196-9781 CODEN: PEPTDO
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 003 Endocrinology
026 Immunology, Serology and Transplantation
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB D-Amino acid substitutions in the anti-inflammatory/antipyretic Ac-.alpha.-MSH(11-13)-NH2 tripeptide of Ac-.alpha.-MSH(1-13)-NH2 were made and the altered peptides were injected in mice treated with picryl chloride. Ear swelling, measured 3 and 6 h after application of the irritant, was reduced by IP injections of Ac-.alpha.-MSH(11-13)-NH2, in confirmation of previous observations. Ac-[D-Lys11].alpha.-MSH(11-13)-NH2 effected similar anti-inflammatory activity but Ac-[D-Pro12].alpha.-MSH(11-13)-NH2 was inactive. Ac-[D-Val13].alpha.-MSH(11-13)-NH2 and Ac-[D-Lys11,D-Val13].alpha.-MSH(11-13)-NH2 generally had greater anti-inflammatory activity than the parent tripeptide molecule; the dose-response relations exhibited the bell-shaped characteristics seen previously with MSH peptides. The results indicate that the L-Pro12 is essential for the anti-inflammatory activity of Ac-.alpha.-MSH(11-13)-NH2 whereas the L-Lys11 is not. D-Val13 substitution increased anti-inflammatory activity approximately four-fold over Ac-.alpha.-MSH(11-13)-NH2. These results provide new structure-activity relationships of the anti-inflammatory Ac-.alpha.-MSH(11-13)-NH2 molecule. The data support the developing idea that .alpha.-MSH and its COOH-terminal fragments modulate host responses, perhaps by antagonizing the actions of cytokines.
SO Peptides, (1991) 12/4 (767-771).
ISSN: 0196-9781 CODEN: PEPTDO

AB D-Amino acid substitutions in the anti-inflammatory/antipyretic Ac-.alpha.-MSH(11-13)-NH2 tripeptide of Ac-.alpha.-MSH(1-13)-NH2 were made and the altered peptides were injected in mice treated with picryl chloride. Ear swelling, measured 3 and 6 h after application of the irritant, . . .

CT Medical Descriptors:
*immune response
*inflammation: DT, drug therapy
animal experiment
animal model
article
controlled study
female
intrapерitoneal drug administration
mouse
nonhuman
priority journal
*alpha intermedin: PD, pharmacology
*alpha intermedin: AN, drug analysis
*alpha intermedin derivative: PD, pharmacology
*alpha intermedin derivative: AN, drug analysis
*picryl. . .

L4 ANSWER 10 OF 11 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 90181611 EMBASE
DOCUMENT NUMBER: 1990181611
TITLE: Peptidergic control of cardiovascular function: The angiotensin paradigm.
AUTHOR: Ganten D.
CORPORATE SOURCE: Inst. High Blood Pressure Res., Im Neuenheimer Feld 366, D-6900 Heidelberg 1, Germany
SOURCE: European Heart Journal, (1990) 11/SUPPL. B (72-78).
ISSN: 0195-668X CODEN: EHJODF
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 002 Physiology
003 Endocrinology
008 Neurology and Neurosurgery
018 Cardiovascular Diseases and Cardiovascular Surgery
LANGUAGE: English
SUMMARY LANGUAGE: English

AB If we consider the chemical messengers in the central nervous system, there are about ten classic transmitters - the catecholamines, biogenic amines and amino acids - as opposed to over 50 different neuropeptides. These include previously well-established circulating hormones such as angiotensin, atrial natriuretic peptide, vasopressin and oxytocin, calcitonin and calcitonin gene related peptide (CGRP), the opioid family of peptides, gastrointestinal peptides, pituitary peptides and their releasing factors, and miscellaneous peptides such as the kinins, bombesin, gallanin, and others; all occur as neuropeptides in the brain. There is evidence supporting a role in central cardiovascular control for angiotensin, opioid peptides, substance P, neuropeptide Y, vasopressin, atrial natriuretic peptide, kinins, corticotropin releasing factor bombesin, somatostatin, and some other peptides. They have been localized in brain areas known to be important for blood pressure regulation, and specific high-affinity peptide receptors have also been discovered. Upon central administration, these peptides produce cardiovascular effects, partly by interacting with other blood pressure-controlling neuroregulators, e.g. catecholamines and GABA. Central inhibition of brain peptide synthesis or interaction with competitive antagonists at the receptor site results in marked cardiovascular effects. Altered peptide levels and activity of synthesizing enzymes, as well as supersensitivity to the pressor action of some brain peptides, have been described in experimental models of hypertension. We are using angiotensin as a model peptide to study the peptidergic control of cardiovascular

function.
 SO European Heart Journal, (1990) 11/SUPPL. B (72-78).
 ISSN: 0195-668X CODEN: EHJODF
 AB . . . areas known to be important for blood pressure regulation, and specific high-affinity peptide receptors have also been discovered. Upon central administration, these peptides produce cardiovascular effects, partly by interacting with other blood pressure-controlling neuroregulators, e.g. catecholamines and GABA. Central inhibition of brain peptide synthesis or interaction with competitive antagonists at the receptor site results in marked cardiovascular effects. **Altered peptide** levels and activity of synthesizing enzymes, as well as supersensitivity to the pressor action of some brain peptides, have been.

L4 ANSWER 11 OF 11 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
 ACCESSION NUMBER: 87160027 EMBASE
 DOCUMENT NUMBER: 1987160027
 TITLE: Weight change and peptide hormone responses in patients receiving interferon.
 AUTHOR: Hurley R.S.; O'Dorisio T.M.; Bossetti B.M.; et al.
 CORPORATE SOURCE: Division of Hematology and Oncology, College of Medicine, The Ohio State University, Columbus, OH 43210, United States
 SOURCE: Nutrition and Cancer, (1987) 10/1-2 (89-94).
 CODEN: NUCADQ
 COUNTRY: United States
 DOCUMENT TYPE: Journal
 FILE SEGMENT: 037 Drug Literature Index
 038 Adverse Reactions Titles
 017 Public Health, Social Medicine and Epidemiology
 003 Endocrinology
 016 Cancer
 LANGUAGE: English

AB The purpose of this pilot study was to describe body weight status and peptide hormone responses in patients receiving interferon (IFN) therapy for renal cell carcinoma. Eighteen patients were on therapy for approximately two to three months. Mean weight loss of the patients was 2.2 +/- 0.9 kg (mean +/- SEM) or 4.9 +/- 0.9% of prestudy weight. Of the 18 patients, 6 were further evaluated for peptide hormone responses to meal stimulation before and after treatment (mean: 1.5 months). These subjects had a mean weight loss of 4.3 +/- 1.6 kg or 7.0 +/- 3.5% of prestudy weight. Blood was drawn from subjects before and six times after they had consumed a defined formula liquid meal to provoke enteroinsular peptide release. It was discovered that one-half of this group (n = 3; Group A) had some glucose intolerance following IFN therapy, despite increased response of insulin, gastric inhibitory polypeptide (GIP), and pancreatic polypeptide (PP) to meal stimulation. Further, patients in Group A had a weight loss of -11.7 +/- 2.7% of prestudy weight, whereas the other three patients (Group B) experienced a mean loss of -2.3 +/- 1.2% (p < 0.04). The three subjects characterized by the smaller loss of prestudy weight (Group B) had decreased glucose response to meal stimulation, despite decreased responses of insulin and GIP. Response of PP was slightly increased with treatment in group B, but the increase was not as large as that in Group A. These data may suggest that extreme weight loss and **altered peptide** hormone response occur in a subset of cancer patients receiving interferon therapy.

SO Nutrition and Cancer, (1987) 10/1-2 (89-94).
 CODEN: NUCADQ
 AB . . . the increase was not as large as that in Group A. These data may suggest that extreme weight loss and **altered peptide** hormone response occur in a subset of cancer patients receiving interferon therapy.

CT Medical Descriptors:
 *adverse drug reaction
 *body weight
 *cancer immunotherapy
 *glucose intolerance
 *hormone release
 *immunotherapy
 *kidney cancer
 *drug therapy
 *weight reduction
 priority journal
 endocrine system
 therapy
 subcutaneous drug administration
 human
 clinical article
 *beta interferon
 *gamma interferon
 *interferon
 *peptide hormone

=> s Landry S?/au
 L5 472 LANDRY S?/AU

=> s 15 and peptide
 L6 56 L5 AND PEPTIDE

=> dup rem 16
 PROCESSING COMPLETED FOR L6
 L7 27 DUP REM L6 (29 DUPLICATES REMOVED)

=> dis 17 1-27 ibib abs kwic

L7 ANSWER 1 OF 27 MEDLINE DUPLICATE 1
 ACCESSION NUMBER: 2001454958 MEDLINE
 DOCUMENT NUMBER: 21391908 PubMed ID: 11395498
 TITLE: The disordered mobile loop of GroES folds into a defined beta-hairpin upon binding GroEL.
 AUTHOR: Shewmaker F; Maskos K; Simmerling C; Landry S J
 CORPORATE SOURCE: Department of Biochemistry, Tulane University Health Sciences Center, New Orleans, Louisiana 70112-2699, USA.
 SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (2001 Aug 17) 276 (33) 31257-64.
 Journal code: HIV; 2985121R. ISSN: 0021-9258.
 PUB. COUNTRY: United States
 LANGUAGE: English
 FILE SEGMENT: Journal; Article; (JOURNAL ARTICLE)
 ENTRY MONTH: 200109
 ENTRY DATE: Entered STN: 20010814

Last Updated on STN: 2001091
Entered Medline: 20010906

AB The GroES mobile loop is a stretch of approximately 16 amino acids that exhibits a high degree of flexible disorder in the free protein. This loop is responsible for the interaction between GroES and GroEL, and it undergoes a folding transition upon binding to GroEL. Results derived from a combination of transferred nuclear Overhauser effect NMR experiments and molecular dynamics simulations indicate that the mobile loop adopts a beta-hairpin structure with a Type I, G1 Bulge turn. This structure is distinct from the conformation of the loop in the co-crystal of GroES with GroEL-ADP but identical to the conformation of the bacteriophage-panned "strongly binding peptide" in the co-crystal with GroEL. Analysis of sequence conservation suggests that sequences of the mobile loop and strongly binding peptide were selected for the ability to adopt this hairpin conformation.

AU Shewmaker F; Maskos K; Simmerling C; Landry S J

AB . . . of the loop in the co-crystal of GroES with GroEL-ADP but identical to the conformation of the bacteriophage-panned "strongly binding peptide" in the co-crystal with GroEL. Analysis of sequence conservation suggests that sequences of the mobile loop and strongly binding peptide were selected for the ability to adopt this hairpin conformation.

L7 ANSWER 2 OF 27 BIOSIS COPYRIGHT 2001 BIOSIS

ACCESSION NUMBER: 2001:258563 BIOSIS

DOCUMENT NUMBER: PREV200100258563

TITLE: Direct ex vivo characterization of gp120-specific CD4 and CD8 T cells in HIV-infected and healthy donors using immunospot assays.

AUTHOR(S): Kleen, Thomas (1); Assad, Robert (1); Landry, Samuel; Tary-Lehmann, Magdalena (1)

CORPORATE SOURCE: (1) Case Western Reserve University, New Orleans, LA, 70112 USA

SOURCE: FASEB Journal, (March 8, 2001) Vol. 15, No. 5, pp. A1228. print.
Meeting Info.: Annual Meeting of the Federation of American Societies for Experimental Biology on Experimental Biology 2001 Orlando, Florida, USA March 31-April 04, 2001
ISSN: 0892-6638.

DOCUMENT TYPE: Conference

LANGUAGE: English

SUMMARY LANGUAGE: English

AB The full range of HIV peptides (determinants) that are targeted by memory T cells is presently not known, nor is the magnitude and cytokine quality of the T cell responses involved. Towards this end, we performed systematic determinant mapping with gp120 peptides involving a new generation of image-analysis assisted ELISPOT assays. A 20-mer peptides series was used that walks the entire gp 120 molecule in steps of 10 amino acids. We measured IFN-gamma and granzyme B production in response to these peptides. We found that all seven patients tested responded to several peptides (2 - 13) and typically involving frequencies > 100/million. In contrast, only one of the five healthy controls showed a response that involved a comparable frequency of T cells, and this response was confined to a single peptide (consistent with crossreactive recognition). All of the patient responded with granzyme B production against minimum one to maximum 9 different peptides. Cell separation experiments showed that the IFN-gamma-producing cells elicited by the 20-mer peptides resided in the CD4 and the CD8 cell compartment. In contrast, the granzyme B-recall responses were confined to the CD8 fraction. The data show the feasibility of systematic assessment of HIV-specific CD4 and CD8 cell immunity in HIV infected patients.

AU Kleen, Thomas (1); Assad, Robert (1); Landry, Samuel;
Tary-Lehmann, Magdalena (1)

AB The full range of HIV peptides (determinants) that are targeted by memory T cells is presently not known, nor is the magnitude and cytokine quality of the T cell responses involved. Towards this end, we performed systematic determinant mapping with gp120 peptides involving a new generation of image-analysis assisted ELISPOT assays. A 20-mer peptides series was used that walks the entire gp 120 molecule in steps of 10 amino acids. We measured IFN-gamma and granzyme B production in response to these peptides. We found that all seven patients tested responded to several peptides (2 - 13) and typically involving frequencies > 100/million. In contrast, only one of the five healthy controls showed a response that involved a comparable frequency of T cells, and this response was confined to a single peptide (consistent with crossreactive recognition). All of the patient responded with granzyme B production against minimum one to maximum 9 different peptides. Cell separation experiments showed that the IFN-gamma-producing cells elicited by the 20-mer peptides resided in the CD4 and the CD8 cell compartment. In contrast, the granzyme B-recall responses were confined to the CD8.

L7 ANSWER 3 OF 27 MEDLINE

ACCESSION NUMBER: 2000183814 MEDLINE

DOCUMENT NUMBER: 20183814 PubMed ID: 10716904

TITLE: Helper T-cell epitope immunodominance associated with structurally stable segments of hen egg lysozyme and HIV gp120.

AUTHOR: Landry S J

CORPORATE SOURCE: Department of Biochemistry, Tulane University School of Medicine, 1430 Tulane Avenue, New Orleans, LA 70112, USA..
landry@mailhost.tcs.tulane.edu

CONTRACT NUMBER: R01AI42350 (NIAID)

R21AI42702 (NIAID)

SOURCE: JOURNAL OF THEORETICAL BIOLOGY, (2000 Apr 7) 203 (3) 189-201.

Journal code: K8N; 0376342. ISSN: 0022-5193.

PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200004

ENTRY DATE: Entered STN: 20000505

Last Updated on STN: 20000505

Entered Medline: 20000426

AB Although many antigen sequences potentially can bind to the MHCII proteins, only a small number of epitopes dominate the immune response. Additional mechanisms of processing, presentation or recognition must restrict the immune response against a large portion of the antigen. A highly significant correlation is found between epitope immunodominance and local structural stability in hen egg lysozyme. Since antigen proteins are likely to retain substantial native-like structure in the processing

compartment, protease action may be focused on regions that are most readily accommodated in the protease active sites, and thus, the intervening sequence are preferentially presented. Immunodominance also correlates with sequence conservation as expected from the constraints imposed by structure. These results suggest that the three-dimensional structure of the antigen limits the immune response against some antigen segments. For HIV gp120, a substantial improvement in the accuracy of epitope prediction is obtained by combining rules for MHCII binding with a restriction of the predicted epitopes to well-conserved sequences.

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AU Landry S J

CT

Protein gp120: IM, immunology
Histocompatibility Antigens Class II: IM, immunology
*Immunodominant Epitopes: IM, immunology

*Muramidase: GE, genetics

Muramidase: IM, immunology

*Peptide Fragments: GE, genetics

Peptide Fragments: IM, immunology

*T-Lymphocytes, Helper-Inducer: IM, immunology

CN 0 (HIV Envelope Protein gp120); 0 (Histocompatibility Antigens Class II);
0 (Immunodominant Epitopes); 0 (Peptide Fragments); 0 (hen egg
lysozyme peptide (50-62)); EC 3.2.1.17 (Muramidase)

L7 ANSWER 4 OF 27 MEDLINE DUPLICATE 2

ACCESSION NUMBER: 1999435726 MEDLINE

DOCUMENT NUMBER: 99435726 PubMed ID: 10504222

TITLE: Basis of substrate binding by the chaperonin GroEL.

AUTHOR: Wang Z; Feng H p; Landry S J; Maxwell J; Gierasch

L M

CORPORATE SOURCE: Department of Chemistry, University of Massachusetts,
Amherst, Massachusetts 01003, USA.

CONTRACT NUMBER: GM27616 (NIGMS)

SOURCE: BIOCHEMISTRY, (1999 Sep 28) 38 (39) 12537-46.

Journal code: AOG; 0370623. ISSN: 0006-2960.

PUB. COUNTRY: United States

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199910

ENTRY DATE: Entered STN: 19991101

Last Updated on STN: 19991101

Entered Medline: 19991020

AB The molecular chaperonins are essential proteins involved in protein folding, complex assembly, and polypeptide translocation. While there is abundant structural information about the machinery and the mechanistic details of its action are well studied, it is yet unresolved how chaperonins recognize a large number of structurally unrelated polypeptides in their unfolded or partially folded forms. To determine the nature of chaperonin-substrate recognition, we have characterized by NMR methods the interactions of GroEL with synthetic peptides that mimic segments of unfolded proteins. In previous work, we found using transferred nuclear Overhauser effect (trNOE) analysis that two 13 amino acid peptides bound GroEL in an amphipathic alpha-helical conformation. By extending the study to a variety of peptides with differing sequence motifs, we have observed that peptides can adopt conformations other than alpha-helix when bound to GroEL. Furthermore, peptides of the same composition exhibited significantly different affinities for GroEL as manifested by the magnitude of trNOEs. Binding to GroEL correlates well with the ability of the peptide to cluster hydrophobic residues on one face of the peptide, as determined by the retention time on reversed-phase (RP) HPLC. We conclude that the molecular basis of GroEL-substrate recognition is the presentation of a hydrophobic surface by an incompletely folded polypeptide and that many backbone conformations can be accommodated.

AU Wang Z; Feng H p; Landry S J; Maxwell J; Gierasch L M

AB . . . forms. To determine the nature of chaperonin-substrate recognition, we have characterized by NMR methods the interactions of GroEL with synthetic peptides that mimic segments of unfolded proteins. In previous work, we found using transferred nuclear Overhauser effect (trNOE) analysis that two 13 amino acid peptides bound GroEL in an amphipathic alpha-helical conformation. By extending the study to a variety of peptides with differing sequence motifs, we have observed that peptides can adopt conformations other than alpha-helix when bound to GroEL. Furthermore, peptides of the same composition exhibited significantly different affinities for GroEL as manifested by the magnitude of trNOEs. Binding to GroEL correlates well with the ability of the peptide to cluster hydrophobic residues on one face of the peptide, as determined by the retention time on reversed-phase (RP) HPLC. We conclude that the molecular basis of GroEL-substrate recognition is. . .

L7 ANSWER 5 OF 27 MEDLINE DUPLICATE 3

ACCESSION NUMBER: 1998263316 MEDLINE

DOCUMENT NUMBER: 98263316 PubMed ID: 9600925

TITLE: Role of the J-domain in the cooperation of Hsp40 with Hsp70.

AUTHOR: Greene M K; Maskos K; Landry S J

CORPORATE SOURCE: Department of Biochemistry, Tulane University School of
Medicine, New Orleans, LA 70112-2699, USA.

SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE
UNITED STATES OF AMERICA, (1998 May 26) 95 (11) 6108-13.

Journal code: PV3; 7505876. ISSN: 0027-8424.

PUB. COUNTRY: United States

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199806

ENTRY DATE: Entered STN: 19980708

Last Updated on STN: 19980708

Entered Medline: 19980622

AB The Escherichia coli Hsp40 DnaJ and Hsp70 DnaK cooperate in the binding of proteins at intermediate stages of folding, assembly, and translocation across membranes. Binding of protein substrates to the DnaK C-terminal domain is controlled by ATP binding and hydrolysis in the N-terminal ATPase domain. The interaction of DnaJ with DnaK is mediated at least in part by the highly conserved N-terminal J-domain of DnaJ that includes residues 2-75. Heteronuclear NMR experiments with uniformly ¹⁵N-enriched DnaJ2-75 indicate that the chemical environment of residues located in helix II and the flanking loops is perturbed on interaction with DnaK or a truncated DnaK molecule, DnaK2-388. NMR signals corresponding to these residues broaden and exhibit changes in chemical shifts in the presence of

DnaK(MgADP). Addition of MgATP largely reversed the broadening, indicating that NMR signals of DnaJ2-75 respond to ATP-dependent changes in DnaK. The J-domain interaction is localized to the ATPase domain of DnaK and is likely to be dominated by electrostatic interactions. The results suggest that the J-domain tethers DnaK to DnaJ-bound substrates, which DnaK then binds with its C-terminal **peptide**-binding domain.

AU Greene M K; Maskos K; Landry S J
AB . . . electrostatic interactions. The results suggest that the J-domain tethers DnaK to DnaJ-bound substrates, which DnaK then binds with its C-terminal **peptide**-binding domain.

L7 ANSWER 6 OF 27 BIOSIS COPYRIGHT 2001 BIOSIS

ACCESSION NUMBER: 1999:80640 BIOSIS
DOCUMENT NUMBER: PREV19990080640
TITLE: Evaluation of short C-terminal CGRP antagonists for the CRRP1 receptor subtype.
AUTHOR(S): Landry, S. (1); Dumont, Y. (1); St-Pierre, S.; Quirion, R. (1)
CORPORATE SOURCE: (1) Douglas Hosp. Res. Cent., Dep. Psychiatry, McGill Univ., Montreal, PQ H4H 1R3 Canada
SOURCE: Society for Neuroscience Abstracts, (1998) Vol. 24, No. 1-2, pp. 1592.
Meeting Info.: 28th Annual Meeting of the Society for Neuroscience, Part 2 Los Angeles, California, USA November 7-12, 1998
ISSN: 0190-5295.
DOCUMENT TYPE: Conference
LANGUAGE: English
AU Landry, S. (1); Dumont, Y. (1); St-Pierre, S.; Quirion, R. (1)
IT Major Concepts
Nervous System (Neural Coordination)
IT Chemicals & Biochemicals
calcitonin gene related **peptide** antagonists; calcitonin gene related **peptide** 1 receptor
RN 83652-28-2 (CALCITONIN GENE RELATED **PEPTIDE**)

L7 ANSWER 7 OF 27 MEDLINE DUPLICATE 4

ACCESSION NUMBER: 97428227 MEDLINE
DOCUMENT NUMBER: 97428227 PubMed ID: 9283089
TITLE: Temperature dependence of backbone dynamics in loops of human mitochondrial heat shock protein 10.
AUTHOR: Landry S J; Steede N K; Maskos K
CORPORATE SOURCE: Department of Biochemistry, Tulane University School of Medicine, New Orleans, Louisiana 70112, USA.
SOURCE: BIOCHEMISTRY, (1997 Sep 9) 36 (36) 10975-86.
Journal code: A0G; 0370623. ISSN: 0006-2960.
PUB. COUNTRY: United States
JOURNAL: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199709
ENTRY DATE: Entered STN: 19971013
Last Updated on STN: 19971013
Entered Medline: 19970930

AB A highly flexible, yet conserved polypeptide loop of Hsp10 mediates binding to Hsp60 in the course of chaperonin-dependent protein folding. Previous transferred nuclear Overhauser effect (trNOE) studies with **peptides** based on the mobile loop of the Escherichiacoli and bacteriophage T4 Hsp10s suggested that the mobile loop adopts a characteristic hairpin turn upon binding to the E. coli Hsp60 GroEL. In this paper, we identify the sequence and characterize the nascent structure and dynamics of the 18-residue mobile loop in the 15N-enriched human Hsp10. We also identify four residues of another flexible loop, the roof beta hairpin. The mobile loop and/or roof beta hairpin of several subunits are absent from the X-ray crystal structure of human Hsp10. NMR data suggest that the mobile loop of Hsp10 preferentially samples a hairpin conformation despite the fact that the backbone motion resembles that of a disordered polypeptide. Analysis of backbone dynamics by measurement of 15N relaxation times, T1 and T2, and the 1H-15N nuclear Overhauser effect (1H-15N NOE) indicates that motion is greatest near the center of the loop. Inversion of the temperature dependence of the T1 near the center of the loop marks a transition to motion with a dominant time scale of less than 3 ns. Analysis of the relaxation data by spectral density mapping shows that subnanosecond motion increases uniformly along the loop at elevated temperatures, whereas nanosecond motion increases near the ends of the loop and decreases near the center of the mobile loop. The transition to dominance by fast motion in the center of the loop occurs at a distance from the well-structured part of Hsp10 that is equal to the persistence length of an unstructured polypeptide. Simulation of the spectral density function for the 15N resonance and its temperature dependence using the Lipari-Szabo formalism suggests that the dominant time scales of loop motion range from 0.6 to 18 ns. For comparison, the time scale for molecular rotation of the 70 kDa Hsp10 heptamer is estimated to be 37 ns. Complex behavior of the T2 relaxation time indicates that motion also occurs on longer time scales. All of the modes of loop motion are likely to have an impact on Hsp10/Hsp60 interaction and therefore affect Hsp10/Hsp60 function as a chaperonin.

AU Landry S J; Steede N K; Maskos K
AB . . . Hsp10 mediates binding to Hsp60 in the course of chaperonin-dependent protein folding. Previous transferred nuclear Overhauser effect (trNOE) studies with **peptides** based on the mobile loop of the Escherichiacoli and bacteriophage T4 Hsp10s suggested that the mobile loop adopts a characteristic. . .

L7 ANSWER 8 OF 27 MEDLINE DUPLICATE 5

ACCESSION NUMBER: 97234596 MEDLINE
DOCUMENT NUMBER: 97234596 PubMed ID: 9119033
TITLE: Identification of amino acid residues at nucleotide-binding sites of chaperonin GroEL/GroES and cpn10 by photoaffinity labeling with 2-azido-adenosine 5'-triphosphate.
AUTHOR: Bramhall E A; Cross R L; Rospert S; Steede N K; Landry S J
CORPORATE SOURCE: Department of Biochemistry and Molecular Biology, State University of New York, Health Science Center at Syracuse 13210, USA.
CONTRACT NUMBER: GM23152 (NIGMS)
SOURCE: EUROPEAN JOURNAL OF BIOCHEMISTRY, (1997 Mar 1) 244 (2) 627-34.
Journal code: EMZ; 0107600. ISSN: 0014-2956.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
JOURNAL: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals

ENTRY MONTH: 199704
ENTRY DATE: Entered STN: 19970506
Last Updated on STN: 19970506
Entered Medline: 19970422

AB Although the chaperonin GroEL/GroES complex binds and hydrolyzes ATP, its structure is unlike other known ATPases. In order to better characterize its nucleotide binding sites, we have photolabeled the complex with the affinity analog 2-azido-ATP. Three residues of GroEL, Prol37, Cys138 and Thr468, are labeled by the probe. The location of these residues in the GroEL crystal structure [Braig, K., Otwinowski, Z., Hedge, R., Boisvert, D., Joachimiak, A., Horwich, A. & Sigler, P. (1994) Nature 371, 578-586; Boisvert, D. C., Wang, J., Otwinowski, Z., Horwich, A. L. & Sigler, P. B. (1996) Nat. Struct. Biol. 3, 170-177] suggests that 2-azido-ATP binds to an alternative conformer of GroEL in the presence of GroES. The labeled site appears to be located at the GroEL/GroEL subunit interface since modification of Prol37 and Cys138 is most readily explained by attack of a probe molecule bound to the adjacent GroEL subunit. Labeling of the co-chaperonin, GroES, is clearly demonstrated on gels and the covalent tethering of nucleotide allows detection of a GroES dimer in the presence of SDS. However, no stable peptide derivative of GroES could be purified for sequencing. In contrast, the GroES homolog, yeast cpn10, does give a stable derivative. The modified amino acid is identified as the conserved Prol3, which corresponds to Pro5 in Escherichia coli GroES.

AU Bramhall E A; Cross R L; Rospert S; Steede N K; Landry S J
AB . . . and the covalent tethering of nucleotide allows detection of a GroES dimer in the presence of SDS. However, no stable peptide derivative of GroES could be purified for sequencing. In contrast, the GroES homolog, yeast cpn10, does give a stable derivative.. . .

L7 ANSWER 9 OF 27 MEDLINE
ACCESSION NUMBER: 1998047507 MEDLINE
DOCUMENT NUMBER: 98047507 PubMed ID: 9386348
TITLE: Local protein instability predictive of helper T-cell epitopes.
AUTHOR: Landry S J
CORPORATE SOURCE: Dept of Biochemistry, Tulane University School of Medicine, New Orleans, LA 70112, USA.. landry@mailhost.tcs.tulane.edu
SOURCE: IMMUNOLOGY TODAY, (1997 Nov) 18 (11) 527-32. Ref: 32
Journal code: AEA; 8008346. ISSN: 0167-5699.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199801
ENTRY DATE: Entered STN: 19980206
Last Updated on STN: 19980206
Entered Medline: 19980126

AB Although selectivity at the levels of peptide binding to major histocompatibility complex (MHC) class II and recognition by T cells may partially account for immunodominance patterns, it is clear that differential antigen processing also exerts a strong effect. Here, Sam Landry correlates immunodominant epitopes with nearby structurally unstable segments, as identified by hydrogen-deuterium exchange nuclear magnetic resonance (NMR), and suggests that epitope presentation is directed by preferential proteolytic cleavage at the unstable sites.

AU Landry S J
AB Although selectivity at the levels of peptide binding to major histocompatibility complex (MHC) class II and recognition by T cells may partially account for immunodominance patterns, it. . .
CT Crystallography, X-Ray
*Epitopes, T-Lymphocyte: CH, chemistry
*Immunodominant Epitopes: CH, chemistry
Nuclear Magnetic Resonance, Biomolecular
Peptide Mapping
Protein Conformation
*T-Lymphocytes, Helper-Inducer: CH, chemistry
T-Lymphocytes, Helper-Inducer: IM, immunology

L7 ANSWER 10 OF 27 MEDLINE DUPLICATE 6
ACCESSION NUMBER: 97030245 MEDLINE
DOCUMENT NUMBER: 97030245 PubMed ID: 8876186
TITLE: Interplay of structure and disorder in cochaperonin mobile loops.
AUTHOR: Landry S J; Taher A; Georgopoulos C; van der Vies S M
CORPORATE SOURCE: Department of Biochemistry, Tulane University School of Medicine, New Orleans, LA 70112-2699, USA.
SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1996 Oct 15) 93 (21) 11622-7.
Journal code: PV3; 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199612
ENTRY DATE: Entered STN: 19970128
Last Updated on STN: 19970128
Entered Medline: 19961204

AB Protein-protein interactions typically are characterized by highly specific interfaces that mediate binding with precisely tuned affinities. Binding of the Escherichia coli cochaperonin GroES to chaperonin GroEL is mediated, at least in part, by a mobile polypeptide loop in GroES that becomes immobilized in the GroEL/GroES/nucleotide complex. The bacteriophage T4 cochaperonin Gp31 possesses a similar highly flexible polypeptide loop in a region of the protein that shows low, but significant, amino acid similarity with GroES and other cochaperonins. When bound to GroEL, a synthetic peptide representing the mobile loop of either GroES or Gp31 adopts a characteristic bulged hairpin conformation as determined by transferred nuclear Overhauser effects in NMR spectra. Thermodynamic considerations suggest that flexible disorder in the cochaperonin mobile loops moderates their affinity for GroEL to facilitate cycles of chaperonin-mediated protein folding.

AU Landry S J; Taher A; Georgopoulos C; van der Vies S M
AB . . . protein that shows low, but significant, amino acid similarity with GroES and other cochaperonins. When bound to GroEL, a synthetic peptide representing the mobile loop of either GroES or Gp31 adopts a characteristic bulged hairpin conformation as determined by transferred nuclear. . .

CT . . .
ME, metabolism
*GroES Protein: CH, chemistry

*GroES Protein: ME, metabolism
Hydrogen Bonding
Magnetic Resonance Spectroscopy
Models, Molecular
Molecular Sequence Data
Peptide Fragments: CH, chemistry
Peptide Fragments: IP, isolation & purification
Peptide Mapping

*Protein Structure, Secondary
Thermodynamics

CN 0 (GroEL Protein); 0 (GroES Protein); 0 (Peptide Fragments)

L7 ANSWER 11 OF 27 BIOSIS COPYRIGHT 2001 BIOSIS

ACCESSION NUMBER: 1996:310428 BIOSIS

DOCUMENT NUMBER: PREV199699032784

TITLE: Molecular assessment of signal transduction: NMR studies of a synthetic I-kappa-B ankyrin repeat peptide.

AUTHOR(S): Maskos, K.; Landry, S.

CORPORATE SOURCE: Tulane Univ. Sch. Med., New Orleans, LA 70112 USA

SOURCE: FASEB Journal, (1996) Vol. 10, No. 6, pp. A1514.
Meeting Info.: Joint Meeting of the American Society for Biochemistry and Molecular Biology, the American Society for Investigative Pathology and the American Association of Immunologists New Orleans, Louisiana, USA June 2-6, 1996
ISSN: 0892-6638.

DOCUMENT TYPE: Conference

LANGUAGE: English

TI Molecular assessment of signal transduction: NMR studies of a synthetic I-kappa-B ankyrin repeat peptide.

AU Maskos, K.; Landry, S.

L7 ANSWER 12 OF 27 BIOSIS COPYRIGHT 2001 BIOSIS

ACCESSION NUMBER: 1995:137430 BIOSIS

DOCUMENT NUMBER: PREV199598151730

TITLE: Chaperone-substrate interactions.

AUTHOR(S): Gierasch, L. M. (1); Wang, Z.; Hunt, J.; Landry, S.

J.; Feng, E. (1); Deisenhofer, J.

CORPORATE SOURCE: (1) Dep. Chem., Univ. Mass., Amherst, MA 01003 USA

SOURCE: Biophysical Journal, (1995) Vol. 68, No. 2 PART 2, pp. A1.
Meeting Info.: 39th Annual Meeting of the Biophysical Society San Francisco, California, USA February 12-16, 1995
ISSN: 0006-3495.

DOCUMENT TYPE: Conference

LANGUAGE: English

AU Gierasch, L. M. (1); Wang, Z.; Hunt, J.; Landry, S. J.; Feng, E. (1); Deisenhofer, J.

IT Miscellaneous Descriptors

HEAT SHOCK PROTEIN 60; MEETING ABSTRACT; NMR; PEPTIDE FRAGMENTS; PROTEIN FOLDING

L7 ANSWER 13 OF 27 MEDLINE

ACCESSION NUMBER: 95003496 MEDLINE

DOCUMENT NUMBER: 95003496 PubMed ID: 7919795

TITLE: Polypeptide interactions with molecular chaperones and their relationship to in vivo protein folding.

AUTHOR: Landry S J; Gierasch L M

CORPORATE SOURCE: Department of Biochemistry, Tulane University School of Medicine, New Orleans, Louisiana 70112.

CONTRACT NUMBER: GM27616 (NIGMS)

SOURCE: ANNUAL REVIEW OF BIOPHYSICS AND BIOMOLECULAR STRUCTURE, (1994) 23 645-69. Ref: 130
Journal code: BH5; 9211097. ISSN: 1056-8700.

PUB. COUNTRY: United States

Journal; Article; (JOURNAL ARTICLE)

General Review; (REVIEW)

(REVIEW, ACADEMIC)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199411

ENTRY DATE: Entered STN: 19941222

Last Updated on STN: 19941222

Entered Medline: 19941110

AU Landry S J; Gierasch L M

CT

physiology

GroEL Protein: PH, physiology

GroES Protein: PH, physiology

Heat-Shock Proteins 70: PH, physiology

Models, Molecular

*Molecular Chaperones: PH, physiology

*Peptides: ME, metabolism

Protein Conformation

Protein Folding

Protein Structure, Tertiary

Stress: ME, metabolism

Substrate Specificity

CN 0 (Chaperonin 60); 0 (GroEL Protein); 0 (GroES Protein); 0 (Heat-Shock Proteins 70); 0 (Molecular Chaperones); 0 (Peptides)

L7 ANSWER 14 OF 27 MEDLINE

DUPLICATE 7

ACCESSION NUMBER: 93309590 MEDLINE

DOCUMENT NUMBER: 93309590 PubMed ID: 8100614

TITLE: Characterization of a functionally important mobile domain of GroES.

AUTHOR: Landry S J; Zeilstra-Ryalls J; Fayet O;

Georgopoulos C; Gierasch L M

CORPORATE SOURCE: University of Texas Southwestern Medical Center, Dallas 75235-9041.

SOURCE: NATURE, (1993 Jul 15) 364 (6434) 255-8.

Journal code: NSC; 0410462. ISSN: 0028-0836.

PUB. COUNTRY: ENGLAND: United Kingdom

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199308

ENTRY DATE: Entered STN: 19930813

Last Updated on STN: 19950206

Entered Medline: 19930805

AB Although genetic and biochemical evidence has established that GroES is required for the full function of the molecular chaperone, GroEL, little is known about the molecular details of their interaction. GroES enhances the cooperativity of ATP binding and hydrolysis by GroEL (refs 4, 5) and is necessary for release and folding of several GroEL substrates. Here we

report that native GroES has a highly mobile and accessible polypeptide loop whose mobility and accessibility are lost upon formation of the GroES/GroEL complex. In addition, lesions present in eight independently isolated mutant groES alleles map in the mobile loop. Studies with synthetic peptides suggest that the loop binds in a hairpin conformation at a site on GroEL that is distinct from the substrate-binding site. Flexibility may be required in the mobile loops on the GroES seven-mer to allow them to bind simultaneously to sites on seven GroEL subunits, which may themselves be able to adopt different arrangements, and thus to modulate allosterically GroEL/substrate affinity.

AU Landry S J; Zeilstra-Ryalls J; Fayet O; Georgopoulos C; Gierasch L M

AB . . . complex. In addition, lesions present in eight independently isolated mutant groES alleles map in the mobile loop. Studies with synthetic peptides suggest that the loop binds in a hairpin conformation at a site on GroEL that is distinct from the substrate-binding. . . .

CT Protein

*Heat-Shock Proteins: CH, chemistry
Heat-Shock Proteins: GE, genetics
Heat-Shock Proteins: ME, metabolism
Magnetic Resonance Spectroscopy
Molecular Sequence Data
Mutation

Peptide Fragments: CS, chemical synthesis

Peptide Fragments: CH, chemistry

Protein Binding

Protein Conformation

CN 0 (Bacterial Proteins); 0 (DNA, Bacterial); 0 (GroEL Protein); 0 (GroES Protein); 0 (Heat-Shock Proteins); 0 (Peptide Fragments)

L7 ANSWER 15 OF 27 CAPLUS COPYRIGHT 2001 ACS DUPLICATE 8

ACCESSION NUMBER: 1994:265025 CAPLUS

DOCUMENT NUMBER: 120:265025

TITLE: Nuclear magnetic resonance studies of peptides bound to chaperones

AUTHOR(S): Landry, Samuel J.

CORPORATE SOURCE: Sch. Med., Tulane Univ., New Orleans, LA, 70112, USA

SOURCE: Methods (San Diego) (1993), 5(3), 233-41

CODEN: MTHDE9; ISSN: 1046-2023

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The anal. of transferred nuclear Overhauser effects (trNOEs) in NMR spectra provides information about the conformation and mode of binding of small mols. bound to large mols. This technique has been applied to synthetic peptides bound to mol. chaperones, proteins that modulate the folding and assembly of other proteins. Peptides are found to adopt an extended conformation with hsp70 or a helical conformation in assocn. with hsp60, probably reflecting the nature of the resp. chaperone binding sites. In addn., the observation by NMR of a highly mobile internal polypeptide segment in a native protein that regulates hsp60 activity prompted studies on the corresponding synthetic peptide. NMR data show that the mobile segment is nearly as flexible in the native protein as it is the synthetic peptide. This peptide binds to hsp60 in a distinct turn conformation, suggesting that the mobile segment is involved in the hsp60 regulatory function. The trNOE NMR expts. are tech. straightforward and should be applicable to many other systems. Practical aspects of the technique and strategies for optimizing its interpretation are discussed.

TI Nuclear magnetic resonance studies of peptides bound to chaperones

AU Landry, Samuel J.

AB The anal. of transferred nuclear Overhauser effects (trNOEs) in NMR spectra provides information about the conformation and mode of binding of small mols. bound to large mols. This technique has been applied to synthetic peptides bound to mol. chaperones, proteins that modulate the folding and assembly of other proteins. Peptides are found to adopt an extended conformation with hsp70 or a helical conformation in assocn. with hsp60, probably reflecting the nature of the resp. chaperone binding sites. In addn., the observation by NMR of a highly mobile internal polypeptide segment in a native protein that regulates hsp60 activity prompted studies on the corresponding synthetic peptide. NMR data show that the mobile segment is nearly as flexible in the native protein as it is the synthetic peptide. This peptide binds to hsp60 in a distinct turn conformation, suggesting that the mobile segment is involved in the hsp60 regulatory function. The trNOE NMR expts. are tech. straightforward and should be applicable to many other systems. Practical aspects of the technique and strategies for optimizing its interpretation are discussed.

ST NMR synthetic peptide binding chaperone

IT Peptides, biological studies

RL: BIOL (Biological study)

(binding of synthetic, to chaperones, NMR of)

IT Conformation and Conformers

(of protein-bound synthetic peptides)

IT Overhauser spectrometry

(transferred nuclear, of synthetic peptides bound to chaperones)

IT Proteins, specific or class

RL: ANST (Analytical study)

(hsp 60, chaperones, synthetic peptides bound to, NMR of)

IT Proteins, specific or class

RL: ANST (Analytical study)

(hsp 70, chaperones, synthetic peptides bound to, NMR of)

L7 ANSWER 16 OF 27 BIOSIS COPYRIGHT 2001 BIOSIS

ACCESSION NUMBER: 1993:241879 BIOSIS

DOCUMENT NUMBER: PREV199344115079

TITLE: Using peptides to explore how proteins are folded and sorted in vivo.

AUTHOR(S): Gierasch, L. M.; Landry, S. J.; Maxwell, J.; Scott, T.; Triplett, T. L.; Zheng, N.; Bansal, A.; Kibbey, R.

CORPORATE SOURCE: Univ. Tex. Southwest. Med. Cent., Dallas, TX 75235-9041 USA

SOURCE: Journal of Cellular Biochemistry Supplement, (1993) Vol. 0, No. 17 PART C, pp. 210.
Meeting Info.: Keystone Symposium on Prospects and Progress in Drug Design Based on Peptides and Proteins Taos, New Mexico, USA March 8-14, 1993
ISSN: 0733-1959.

DOCUMENT TYPE: Conference

LANGUAGE: English
 TI Using **peptides** to explore how proteins are folded and sorted in vivo.
 AU Gierasch, L. M.; Landry, S. J.; Maxwell, J.; Scott, T.; Triplett, T. L.; Zheng, N.; Bansal, A.; Kibbey, R.

L7 ANSWER 17 OF 27 MEDLINE DUPLICATE 9
 ACCESSION NUMBER: 92131133 MEDLINE
 DOCUMENT NUMBER: 92131133 PubMed ID: 1346469
 TITLE: Different conformations for the same polypeptide bound to chaperones DnaK and GroEL.
 AUTHOR: Landry S J; Jordan R; McMacken R; Gierasch L M
 CORPORATE SOURCE: Department of Pharmacology, University of Texas Southwestern Medical Center, Dallas 75325-9041.
 SOURCE: NATURE, (1992 Jan 30) 355 (6359) 455-7.
 JOURNAL code: NSC; 0410462. ISSN: 0028-0836.
 PUB. COUNTRY: ENGLAND: United Kingdom
 JOURNAL; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 199203
 ENTRY DATE: Entered STN: 19920322
 Last Updated on STN: 19950206
 Entered Medline: 19920303

AB The proteins DnaK (hsp70) and GroEL (cpn60) from Escherichia coli are prototypes of two classes of molecular chaperones conserved throughout evolution. The analysis of transferred nuclear Overhauser effects in two-dimensional NMR spectra is ideally suited to determine chaperone-bound conformations of **peptides**. The **peptide** vsv-C (amino-acid sequence KLIGVLSSLFRPK) stimulates the ATPase of BiP and Hsc70 (ref. 3) and the intrinsic ATPase of DnaK. The affinity of the vsv-C **peptide** for DnaK is greatly reduced in the presence of ATP. Here we analyse transferred nuclear Overhauser effects and show that the **peptide** is in an extended conformation while bound to DnaK but is helical when bound to GroEL. NMR also indicates that the mobility of the **peptide** backbone is reduced more by binding to DnaK than by binding to GroEL, whereas the side chains are less mobile when bound to GroEL.

AU Landry S J; Jordan R; McMacken R; Gierasch L M
 AB . . . evolution. The analysis of transferred nuclear Overhauser effects in two-dimensional NMR spectra is ideally suited to determine chaperone-bound conformations of **peptides**. The **peptide** vsv-C (amino-acid sequence KLIGVLSSLFRPK) stimulates the ATPase of BiP and Hsc70 (ref. 3) and the intrinsic ATPase of DnaK. The affinity of the vsv-C **peptide** for DnaK is greatly reduced in the presence of ATP. Here we analyse transferred nuclear Overhauser effects and show that the **peptide** is in an extended conformation while bound to DnaK but is helical when bound to GroEL. NMR also indicates that the mobility of the **peptide** backbone is reduced more by binding to DnaK than by binding to GroEL, whereas the side chains are less mobile. . .

L7 ANSWER 18 OF 27 CAPLUS COPYRIGHT 2001 ACS
 ACCESSION NUMBER: 1993:54509 CAPLUS
 DOCUMENT NUMBER: 118:54509
 TITLE: Recognition of **peptides** by the E. coli molecular chaperones, GroEL and DnaK
 AUTHOR(S): Landry, Samuel J.; Gierasch, Lila M.
 CORPORATE SOURCE: Southwest. Med. Cent., Univ. Texas, Dallas, TX, 75235-9041, USA
 SOURCE: Pept.: Chem. Biol., Proc. Am. Pept. Symp., 12th (1992), Meeting Date 1991, 206-8. Editor(s): Smith, John A.; Rivier, Jean E.
 ESCOM: Leiden, Neth.
 CODEN: 57XGA9
 DOCUMENT TYPE: Conference
 LANGUAGE: English

AB In the present study, the interaction of a **peptide** (vsv-C), corresponding to a sequence from the vesicular stomatitis virus G protein, with both GroEL and DnaK was compared. The results demonstrate that the same **peptide** sequence binds to the 2 different mol. chaperones; however, the conformation of the **peptide** is distinct in its 2 binding interactions.

TI Recognition of **peptides** by the E. coli molecular chaperones, GroEL and DnaK

AU Landry, Samuel J.; Gierasch, Lila M.
 AB In the present study, the interaction of a **peptide** (vsv-C), corresponding to a sequence from the vesicular stomatitis virus G-protein, with both GroEL and DnaK was compared. The results demonstrate that the same **peptide** sequence binds to the 2 different mol. chaperones; however, the conformation of the **peptide** is distinct in its 2 binding interactions.

ST chaperone GroEL DnaK **peptide** vsvC
 IT Conformation and Conformers
 (of **peptide** vsv-C bound to chaperone GroEL and DnaK of Escherichia coli)
 IT Proteins, specific or class
 RL: BIOL (Biological study)
 (DnaK, **peptide** vsv-C interaction with, of Escherichia coli)
 IT Proteins, specific or class
 RL: BIOL (Biological study)
 (chaperonins 60, **peptide** vsv-C interaction with, of Escherichia coli)

L7 ANSWER 19 OF 27 BIOSIS COPYRIGHT 2001 BIOSIS
 ACCESSION NUMBER: 1992:402343 BIOSIS
 DOCUMENT NUMBER: BR43:58218
 TITLE: RECOGNITION OF **PEPTIDES** BY THE ESCHERICHIA-COLI MOLECULAR CHAPERONES GROEL AND DNAK.
 AUTHOR(S): LANDRY S J; GIERASCH L M
 CORPORATE SOURCE: DEP. PHARMACOL., UNIV. TEX. SOUTHWESTERN MED. CENT., DALLAS, TEX. 75235-9041, USA.
 SOURCE: SMITH, J. A. AND J. E. RIVIER (ED.). PEPTIDES: CHEMISTRY AND BIOLOGY; TWELFTH AMERICAN PEPTIDE SYMPOSIUM, CAMBRIDGE, MASSACHUSETTS, USA, JUNE 16-21, 1991. LVIII+989P. ESCOM SCIENCE PUBLISHERS B.V.: LEIDEN, NETHERLANDS. ILLUS, (1992) 0 (0), 206-208.
 ISBN: 90-72199-12-X.
 DOCUMENT TYPE: Conference
 FILE SEGMENT: BR; OLD
 LANGUAGE: English
 TI RECOGNITION OF **PEPTIDES** BY THE ESCHERICHIA-COLI MOLECULAR CHAPERONES GROEL AND DNAK.
 AU LANDRY S J; GIERASCH L M

L7 ANSWER 20 OF 27 CAPLUS COPYRIGHT 2001 ACC DUPLICATE 10
 ACCESSION NUMBER: 1992:230265 CAPLUS
 DOCUMENT NUMBER: 116:230265
 TITLE: Biophysical studies of recognition sequences for targeting and folding
 AUTHOR(S): Gierasch, Lila M.; Jones, Jeffrey D.; Landry, Samuel J.; Stradley, Sarah J.
 CORPORATE SOURCE: Southwest. Med. Cent., Univ. Texas, Dallas, TX, 75235-9041, USA
 SOURCE: Antonie van Leeuwenhoek (1992), 61(2), 93-9
 CODEN: ALJMAO; ISSN: 0003-6072
 DOCUMENT TYPE: Journal; General Review
 LANGUAGE: English
 AB A review with 38 refs. on signal sequences required for precursor protein chaperone-mediated folding and for transport targeting. Biophys. studies on the structural determinants for recognition are discussed.
 AU Gierasch, Lila M.; Jones, Jeffrey D.; Landry, Samuel J.; Stradley, Sarah J.
 IT Peptides, biological studies
 RL: BIOL (Biological study)
 (signal, recognition site of, in protein transport, biophys. studies on)

L7 ANSWER 21 OF 27 MEDLINE DUPLICATE 11
 ACCESSION NUMBER: 91308122 MEDLINE
 DOCUMENT NUMBER: 91308122 PubMed ID: 1677268
 TITLE: The chaperonin GroEL binds a polypeptide in an alpha-helical conformation.
 AUTHOR: Landry S J; Gierasch L M
 CORPORATE SOURCE: Department of Pharmacology, University of Texas Southwestern Medical Center, Dallas 75235-9041.
 CONTRACT NUMBER: GM27616 (NIGMS)
 SOURCE: BIOCHEMISTRY, (1991 Jul 30) 30 (30) 7359-62.
 Journal code: AOG; 0370623. ISSN: 0006-2960.
 PUB. COUNTRY: United States
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 199108
 ENTRY DATE: Entered STN: 19910913
 Last Updated on STN: 19950206
 Entered Medline: 19910827
 AB Chaperones facilitate folding and assembly of nascent polypeptides in vivo and prevent aggregation in refolding assays in vitro. A given chaperone acts on a number of different proteins. Thus, chaperones must recognize features present in incompletely folded polypeptide chains and not strictly dependent on primary structural information. We have used transferred nuclear Overhauser effects to demonstrate that the Escherichia coli chaperonin GroEL binds to a peptide corresponding to the N-terminal alpha-helix in rhodanese, a mitochondrial protein whose in vitro refolding is facilitated by addition of GroEL, GroES, and ATP. Furthermore, the peptide, which is unstructured when free in aqueous solution, adopts an alpha-helical conformation upon binding to GroEL. Modification of the peptide to reduce its intrinsic propensity to take up alpha-helical structure lowered its affinity for GroEL, but, nonetheless, it could be bound and took up a helical conformation when bound. We propose that GroEL interacts with sequences in an incompletely folded chain that have the potential to adopt an amphipathic alpha-helix and that the chaperonin binding site promotes formation of a helix.
 AU Landry S J; Gierasch L M
 AB . . . structural information. We have used transferred nuclear Overhauser effects to demonstrate that the Escherichia coli chaperonin GroEL binds to a peptide corresponding to the N-terminal alpha-helix in rhodanese, a mitochondrial protein whose in vitro refolding is facilitated by addition of GroEL, GroES, and ATP. Furthermore, the peptide, which is unstructured when free in aqueous solution, adopts an alpha-helical conformation upon binding to GroEL. Modification of the peptide to reduce its intrinsic propensity to take up alpha-helical structure lowered its affinity for GroEL, but, nonetheless, it could be.

L7 ANSWER 22 OF 27 BIOSIS COPYRIGHT 2001 BIOSIS
 ACCESSION NUMBER: 1991:355478 BIOSIS
 DOCUMENT NUMBER: BR41:39993
 TITLE: A SYNTHETIC PEPTIDE DERIVED FROM RHODANESE FORMS A HELIX IN ASSOCIATION WITH THE CHAPERONIN GROEL.
 AUTHOR(S): LANDRY S J; MENDOZA J; HOROWITZ P M; GIERASCH L M
 CORPORATE SOURCE: DEP. PHARMACOL., UT SOUTHWESTERN MED. CENT., DALLAS, TEX. 75235-9041.
 SOURCE: MEETING ON PROTEIN FOLDING, STRUCTURE AND FUNCTION HELD AT THE 20TH ANNUAL MEETING OF THE KEYSTONE SYMPOSIA ON MOLECULAR AND CELLULAR BIOLOGY, KEYSTONE, COLORADO, USA, APRIL 8-14, 1991. J CELL BIOCHEM SUPPL, (1991) 0 (15 PART G), 197.
 CODEN: JCBSD7.
 DOCUMENT TYPE: Conference
 FILE SEGMENT: BR; OLD
 LANGUAGE: English
 TI A SYNTHETIC PEPTIDE DERIVED FROM RHODANESE FORMS A HELIX IN ASSOCIATION WITH THE CHAPERONIN GROEL.
 AU LANDRY S J; MENDOZA J; HOROWITZ P M; GIERASCH L M

L7 ANSWER 23 OF 27 MEDLINE
 ACCESSION NUMBER: 91344277 MEDLINE
 DOCUMENT NUMBER: 91344277 PubMed ID: 1877092
 TITLE: Recognition of nascent polypeptides for targeting and folding.
 AUTHOR: Landry S J; Gierasch L M
 CORPORATE SOURCE: Department of Pharmacology, University of Texas Southwestern Medical Center, Dallas 75235-9041.
 CONTRACT NUMBER: GM27616 (NIGMS)
 GM34962 (NIGMS)
 SOURCE: TRENDS IN BIOCHEMICAL SCIENCES, (1991 Apr) 16 (4) 159-63.
 Ref: 39
 Journal code: WEF; 7610674. ISSN: 0968-0004.
 PUB. COUNTRY: ENGLAND: United Kingdom
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 199109

ENTRY DATE: Entered STN: 19911013
Last Updated on STN: 19911013
Entered Medline: 19910923

AB A major difference between the refolding of proteins in vitro and the in vivo folding process, in which we include localization and assembly, is the need for additional factors in vivo, apart from the protein product itself. Thus, the amino acid sequence of a naturally selected protein contains not only the information specifying its three-dimensional structure, but also the information that enables these factors to recognize the nascent polypeptide. In this review, we consider how this latter information may be encoded and, in turn, interpreted by binding species.

AU Landry S J; Gierasch L M

CT Check Tags: Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
*Bacterial Proteins: GE, genetics
*Peptides: CH, chemistry
*Peptides: GE, genetics
*Protein Conformation
*Protein Processing, Post-Translational

CN 0 (Bacterial Proteins); 0 (Peptides)

L7 ANSWER 24 OF 27 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1991:516660 BIOSIS
DOCUMENT NUMBER: BR41:117375
TITLE: PEPTIDE MODELS FOR PROTEIN FOLDING AND LOCALIZATION.
AUTHOR(S): GIERASCH L M; JONES J D; LANDRY S J; RIZO J; STRADLEY S J; TRIPLETT T L
CORPORATE SOURCE: DEP. PHARMACOL., UNIV. TEX. SOUTHWESTERN MED. CENT., 5323 HARRY HINES BLVD., DALLAS, TEX. 75235-9041.
SOURCE: FOURTH CHEMICAL CONGRESS OF NORTH AMERICA, NEW YORK, NEW YORK, USA, AUGUST 25-30, 1991. ABSTR PAP AM CHEM SOC, (1991) 202 (1-2), BIOL 3.
CODEN: ACSRAL. ISSN: 0065-7727.
DOCUMENT TYPE: Conference
FILE SEGMENT: BR; OLD
LANGUAGE: English
TI PEPTIDE MODELS FOR PROTEIN FOLDING AND LOCALIZATION.
AU GIERASCH L M; JONES J D; LANDRY S J; RIZO J; STRADLEY S J; TRIPLETT T L

L7 ANSWER 25 OF 27 MEDLINE DUPLICATE 12
ACCESSION NUMBER: 89255388 MEDLINE
DOCUMENT NUMBER: 89255388 PubMed ID: 2566610
TITLE: The small subunit of ribulose-1,5-bisphosphate carboxylase/oxygenase and its precursor expressed in Escherichia coli are associated with groEL protein.
AUTHOR: Landry S J; Bartlett S G
CORPORATE SOURCE: Department of Biochemistry, Louisiana State University, Baton Rouge 70803.
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1989 May 25) 264 (15) 9090-3.
PUB. COUNTRY: United States
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198906
ENTRY DATE: Entered STN: 19900306
Last Updated on STN: 19980206
Entered Medline: 19890629

AB The small subunit of ribulose-1,5-bisphosphate carboxylase/oxygenase is synthesized in the cytoplasm as a precursor which is transported into the chloroplast. During or after transport the precursor is processed to its mature size by removal of an amino-terminal transit peptide. Eight small subunits and eight large subunits (synthesized in the chloroplast) assemble to form the holoenzyme. We have expressed the precursor of the small subunit in Escherichia coli as a fusion to the carboxyl terminus of staphylococcal protein A'. The fusion protein was recovered from the bacterial lysate by chromatography on IgG-agarose. A 58-kDa protein copurified with the fusion protein in approximately equal amounts. Much less of the 58-kDa protein copurified with a fusion in which the transit peptide was deleted, and it did not copurify with protein A'. The 58-kDa protein was identified as the E. coli groEL gene product with antibodies directed against a homologous mitochondrial heat shock protein. This finding is particularly interesting because a chloroplast protein involved in the assembly of ribulose-1,5-bisphosphate carboxylase/oxygenase also is homologous to the groEL protein. These homologs could modulate protein-protein interactions during folding and assembly of subunits into native complexes.

AU Landry S J; Bartlett S G

AB . . . the chloroplast. During or after transport the precursor is processed to its mature size by removal of an amino-terminal transit peptide. Eight small subunits and eight large subunits (synthesized in the chloroplast) assemble to form the holoenzyme. We have expressed the . . . fusion protein in approximately equal amounts. Much less of the 58-kDa protein copurified with a fusion in which the transit peptide was deleted, and it did not copurify with protein A'. The 58-kDa protein was identified as the E. coli groEL. . .

L7 ANSWER 26 OF 27 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1988:452471 BIOSIS
DOCUMENT NUMBER: BR35:93351
TITLE: STUDIES ON SYNTHETIC PEPTIDES OF SMALL SUBUNIT OF RIBULOSE-1 5-BISPHOSPHATE CARBOXYLASE RUBISCO.
AUTHOR(S): EDWARDS J V; BLAND J M; CORNELL D G; CLEVELAND T E; LANDRY S; BARLETT S G
CORPORATE SOURCE: USDA, ARS, SRRC, 1100 ROBERT E. LEE BLVD., NEW ORLEANS, LA 70179, USA.
SOURCE: MARSHALL, G. R. (ED.). PEPTIDES: CHEMISTRY AND BIOLOGY; TENTH AMERICAN PEPTIDE SYMPOSIUM, ST. LOUIS, MISSOURI, USA, MAY 23-28, 1987. XXXIII+690P. ESCOM SCIENCE PUBLISHERS B.V.: LEIDEN, NETHERLANDS. ILLUS, (1988) 0 (0), 323-324. ISBN: 90-72199-01-4.
FILE SEGMENT: BR; OLD
LANGUAGE: English
TI STUDIES ON SYNTHETIC PEPTIDES OF SMALL SUBUNIT OF RIBULOSE-1 5-BISPHOSPHATE CARBOXYLASE RUBISCO.
AU EDWARDS J V; BLAND J M; CORNELL D G; CLEVELAND T E; LANDRY S; BARLETT S G

L7 ANSWER 27 OF 27 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1989:473767 CAPLUS

DOCUMENT NUMBER: 111:73767
 TITLE: Studies on synthetic peptides of small subunit of ribulose 1,5-bisphosphate carboxylase (RuBisCO)
 AUTHOR(S): Edwards, Judson V.; Bland, John M.; Cornell, Donald G.; Cleveland, Thomas E.; Landry, Samuel; Bartlett, Susan G.
 CORPORATE SOURCE: SRRC, ARS, New Orleans, LA, 70179, USA
 SOURCE: Pept.: Chem. Biol., Proc. Am. Pept. Symp. 10th (1988), Meeting Date 1987, 323-4. Editor(s): Marshall, Garland R. ESCOM Sci. Pub.: Leiden, Neth. CODEN: 56MDA6
 DOCUMENT TYPE: Conference
 LANGUAGE: English

AB Over 80% of all proteins functional in the chloroplast are post-translationally transported to the organelle. N-terminal presequences (transit peptides) of chloroplast proteins are believed to contain information necessary for import and compartmentalization of the protein. Transit peptides contain 3 major blocks of amino acid homol. The shared blocks may participate in common functions performed by the transit sequence in transport events. In this regard, 3 approaches were taken to examine synthetic transit peptides of the small subunit of RuBisCO (45 residues: block I, residues 1-8; block II, residues 15-20; block III, residues 40-43): (1) a reconstituted chloroplast import assay, (2) monolayer insertion anal., and (3) proteolytic cleavage of intermediate processing block II. Both the in vitro reconstitution bioassay and the monolayer insertion study indicated the probable necessity of the 1st 8-9 residues assocd. with homol. block 1 for chloroplast import of the small subunit of RuBisCO. The protease degrdn. indicated an enzyme specificity for cleavage sites at intermediate processing block II.

TI Studies on synthetic peptides of small subunit of ribulose 1,5-bisphosphate carboxylase (RuBisCO)

AU Edwards, Judson V.; Bland, John M.; Cornell, Donald G.; Cleveland, Thomas E.; Landry, Samuel; Bartlett, Susan G.

AB Over 80% of all proteins functional in the chloroplast are post-translationally transported to the organelle. N-terminal presequences (transit peptides) of chloroplast proteins are believed to contain information necessary for import and compartmentalization of the protein. Transit peptides contain 3 major blocks of amino acid homol. The shared blocks may participate in common functions performed by the transit sequence in transport events. In this regard, 3 approaches were taken to examine synthetic transit peptides of the small subunit of RuBisCO (45 residues: block I, residues 1-8; block II, residues 15-20; block III, residues 40-43): (1) a reconstituted chloroplast import assay, (2) monolayer insertion anal., and (3) proteolytic cleavage of intermediate processing block II. Both the in vitro reconstitution bioassay and the monolayer insertion study indicated the probable necessity of the 1st 8-9 residues assocd. with homol. block 1 for chloroplast import of the small subunit of RuBisCO. The protease degrdn. indicated an enzyme specificity for cleavage sites at intermediate processing block II.

ST ribulose bisphosphate carboxylase subunit transit peptide

IT Biological transport (import, of ribulose bisphosphate carboxylase small subunit, by chloroplast, transit peptide structure and function in)

IT Peptides, biological studies

RL: BIOL (Biological study) (signal, of ribulose bisphosphate carboxylase, function and structure of)

IT 121952-07-6P 121952-08-7P 121986-67-2P 121986-68-3P 121986-69-4P 122071-57-2P

RL: SPN (Synthetic preparation); PREP (Preparation) (prepn. of, as model of transit peptide of ribulose bisphosphate carboxylase small subunit)

IT 9027-23-0, Ribulose 1,5-bisphosphate carboxylase

RL: BIOL (Biological study) (transit peptide of small subunit of, function and structure of)

=> end

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